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STRUCTURE AND FUNCTION

Age-Related Changes in Myocardial Relaxation Using Three-Dimensional Tagged Magnetic Resonance Imaging

Helen C. Oxenham,[1,*] Alistair A. Young,[2] Brett R. Cowan,[3] Thomas L. Gentles,[4] Christopher J. Occleshaw,[3] Carissa G. Fonseca,[2] Robert N. Doughty,[1] and Norman Sharpe[1]

[1]Cardiovascular Research Laboratory, [2]Department of Anatomy with Radiology, and [3]Cardiac MRI Research Group, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand
[4]Paediatric Cardiology, Greenlane Hospital, Auckland, New Zealand

ABSTRACT

Purpose. Marked changes in left ventricular diastolic filling occur with advancing age, but alterations in myocardial movement accompanying these findings have not been previously documented. We aimed to identify differences in myocardial motion during relaxation and diastole using magnetic resonance imaging (MRI), with tagging, which uniquely allows accurate, noninvasive assessment of myocardial movement in three dimensions. *Methods*. Tagged MRI images from two groups of normal individuals were analyzed using dedicated computer software to provide values for group comparison of apical rotation, torsion, and circumferential and longitudinal strain throughout the cardiac cycle. *Results*. The mean age of the younger group was 22 years, ($n = 15$) and that of the older group was 69 years, ($n = 16$). In the older group, peak apical rotation and torsion were increased during systole and significantly more apical rotation, torsion, circumferential, and longitudinal strain persisted during myocardial relaxation and diastole. In addition, peak normalized reversal of apical rotation was reduced ($-5.1 \pm 1.2° s^{-1}$ vs. $-6.7 \pm 1.2° s^{-1}$, $p = 0.001$), and there were slower peak rates of circumferential lengthening ($76.2 \pm 28\%\ s^{-1}$ vs. $142.5 \pm 17\%\ s^{-1}$, $p < 0.001$) and longitudinal lengthening ($62.7 \pm 21\%\ s^{-1}$ vs. $122.5 \pm 20\%\ s^{-1}$, $p < 0.001$). *Conclusions*. Tagged MRI is a unique, noninvasive imaging method that can identify significant prolongation and reduction of myocardial relaxation in older compared with young normal individuals.

Key Words: Aging; Diastolic function; Magnetic resonance imaging (MRI); Myocardial strain.

*Correspondence: Dr. Helen C. Oxenham, Cardiology Department, Royal Infirmary of Edinburgh, 1 Lauriston Place, Edinburgh, EH3 9YW, Scotland; Fax: 00-44-131-536-2021; E-mail: david.oxenham@btinternet.com.

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INTRODUCTION

Advancing age is associated with marked alterations in left ventricular diastolic function whilst left ventricular systolic function at rest is preserved (Lakatta, 1993; Wei, 1992). Studies using echocardiography report a substantial reduction in the peak rate of early diastolic filling between the ages of 30 and 70 years (Benjamin et al., 1992) as well as a prolongation of isovolumetric relaxation time (Lakatta, 1993; Yamakado et al., 1997). The mechanisms underlying these age-related changes are not fully understood but may include decreased Ca^{2+} uptake by the sarcoplasmic reticulum, which results in prolonged myocardial relaxation (Tate et al., 1990). Indirect, noninvasive measurement of transmitral and aortic blood flow (Benjamin et al., 1992; Kitzman et al., 1991) and invasive assessment of left ventricular pressure decay during isovolumetric relaxation (Yamakado et al., 1997) yield conflicting results regarding the changes in myocardial relaxation with aging (Lakatta, 1993; Yamakado et al., 1997). In addition, these techniques are unable to assess the complex, three-dimensional (3D) untwisting motion that occurs during myocardial relaxation and diastole (Stuber et al., 1999). Evaluation of this motion is now possible using magnetic resonance imaging (MRI) with tagging. This technique uses localized saturation of magnetization to label specific regions within the myocardium, creating a grid pattern that is fixed with respect to myocardial tissue and becomes deformed as the myocardium moves. Analysis of this deformation then allows direct, noninvasive measurement of myocardial motion with high accuracy. Unique information is thereby obtained regarding rotational, circumferential, and longitudinal movement through most of the cardiac cycle, and this may provide further insight into age-related changes in diastolic function.

Apical rotation is anticlockwise during systole (viewed from just below the apex, looking towards the base), and clockwise rotation occurs when the myocardium untwists during relaxation and diastole. Previous studies using MRI have described an untwisting motion that occurs primarily during isovolumetric relaxation and have shown it to be a sensitive parameter for the description of myocardial relaxation (Rademakers et al., 1992). This movement has a volume-independent component (Hansen et al., 1991; Moon et al., 1994) and is prolonged in subjects with left ventricular hypertrophy secondary to aortic stenosis (Nagel et al., 2000; Stuber et al., 1999). Age-related changes in myocardial relaxation have not been previously assessed using 3D tagged MRI. The aim of this study was to identify changes in myocardial motion during relaxation and diastole that may account for the marked diastolic changes documented in older people using echocardiography. Older, normal subjects were scanned using tagged MRI, the images analyzed, and the results compared with those from a group of young, normal individuals.

METHODS

Subjects

Subjects were recruited into the study after responding to advertisements within the University of Auckland. The Auckland Human Subjects Ethics Committee approved the study, and all participants gave written, informed consent. After evaluating each subject clinically, a 12-lead echocardiogram (ECG) and transthoracic echocardiogram were performed to exclude important pre-existing cardiac disease or other significant coexisting illness. Exclusion criteria included a history of hypertension, diabetes, ischemic or valvular heart disease, regular medication for cardiovascular illness, a sitting blood pressure above 160/90, or any significant cardiovascular abnormality on physical examination. On the 12-lead ECG, atrial fibrillation, bundle branch block, pathological Q waves, left ventricular hypertrophy, or changes consistent with myocardial ischemia resulted in exclusion, as did any significant valvular abnormality, impaired systolic left ventricular function, or left ventricular hypertrophy on the transthoracic echocardiogram.

Echo Protocol

All patients were examined in the left lateral position using an ATL HDI 5000 echo machine (Bothell, Washington, USA). Images were recorded onto videotape and one person blinded to the group of the subject measured the studies off-line. Measurements were recorded at the end of the expiratory phase of the normal respiratory cycle where indicated and an average value from three recorded measurements was obtained for each echocardiographic parameter. Doppler transmitral inflow velocities were obtained by placing a 5 mm sample volume at the level of the mitral valve annulus with the Doppler beam aligned parallel to the direction of blood flow. The peak early diastolic flow velocity, E wave, the peak transmitral flow velocity in late diastole, A wave, and the ratio of early-to-late diastolic flow velocities, E/A ratio, were all recorded.

MRI Scanning

Patients were scanned using a Siemens 1.5 Tesla Vision MRI scanner using a phased array surface coil. Subjects were scanned in the supine position with approximate 15-second breathholds (at a comfortable position midway between inspiration and expiration according to a standard protocol) to eliminate respiratory motion artifacts. Three scout scans were performed in order to define the long and short axes of the left ventricle. Eight or nine short axis and six long axis imaging planes were then acquired with 15 to 19 time frames per slice. Standard turboFLASH cine MRI images were obtained without tagging (slice thickness 7 mm, in-plane resolution ~1 mm/pixel and temporal resolution of 40 or 50 msec depending on heart rate). Tagged images were then acquired at the same locations as the untagged images and using the same parameters, except for a temporal resolution of 35 or 45 ms (depending on heart rate). All images were prospectively gated; thus, images could not be acquired during the last 10–15% of the cycle to allow for detection of the R wave trigger.

Tagging

Tags are noninvasive myocardial markers that appear as areas with distinctly different signal intensity to the surrounding tissue. Spatial modulation of magnetization (SPAMM) tags were created using nonselective radio frequency pulses separated by gradients, to saturate thin planes of myocardial tissue. Protons in tagged regions are in a different state of magnetization from those in nontagged regions, emit little signal, and appear as black lines in the myocardium. Tagged stripes persist through systole and diastole but fade due to longitudinal relaxation (Table 1) (Axel and Dougherty, 1989).

A specific tagging sequence, spatial modulation of magnetization (SPAMM), using segmented k-space cine imaging with grid tagging on the R wave, was used to create an 8 mm tag grid superimposed on the MRI image (Rademakers and Bogaert, 1997). This grid moves and becomes deformed during cardiac contraction and relaxation. Motion of the grid reflects the motion of myocardial tissue. A representative set of images is shown in Fig. 1.

Analysis of Tagged Images

Images were stored digitally and analyzed off-line using dedicated computer software. Tag stripes within the myocardium were located and tracked using a semiautomated tracking procedure based on an active contour model. Each stripe was subdivided into closely spaced points (two between each stripe intersection) with subpixel resolution in stripe localization. Previous experiments on a silicone model have shown that this method produces accurate, unbiased estimates of displacement and strain (Young et al., 1995). The tagged stripes were tracked through the 15–19 images in each slice to determine the exact position of several hundred points in the myocardium through most of the cardiac cycle. Analysis of this data was performed to identify rotation, torsion, and average strain or percentage

Table 1. Baseline characteristics.

	Young (n = 15) mean (SD)	Old (n = 16) mean (SD)	p value
Age (years)	22.3 (2.6)	68.8 (4.4)	$p < 0.0001$
	Range (19.3–26.2)	Range (60–74)	
Male/Female	11/4	10/6	$p = 0.53$
Weight (kg)	74.4 (15)	74.8 (17.9)	$p = 0.54$
Height (cm)	184.7 (11)	169.5 (8.7)	$p = 0.15$
Heart rate	69.7 (9.8)	70.3 (11.3)	$p = 0.89$
BSA (kg/m^2)	1.83 (0.25)	1.84 (0.25)	$p = 0.99$
Systolic BP (mmHg)	123.5 (14.5)	146 (15.6)	$p < 0.0001$
Diastolic BP (mmHg)	65.5 (5.54)	83.2 (9.92)	$p < 0.0001$
Peak doppler E vel. (m/s)	74.2 (15.9)	46.2 (10)	$p < 0.0001$
Peak doppler A vel. (m/s)	41.3 (7.8)	57.9 (12.5)	$p < 0.0001$

BSA: body surface area.
E = early and A = late peak transmitral flow velocities measured using echo Doppler.

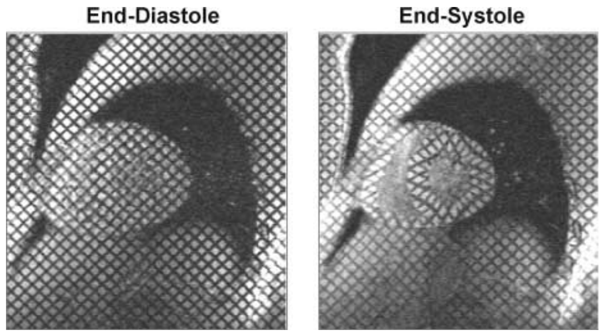

Figure 1. Myocardial tagging. Short axis cardiac images from an older normal individual showing end diastole and end systole.

shortening of the myocardium. Through-plane motion and out of plane shears were accounted for by analyzing the data three-dimensionally.

Left Ventricular Mass and Volumes

Interactive 3D contouring using guide point modeling (Young et al., 1995) was performed to define the epicardial and endocardial contours of the left ventricle on the untagged images and thereby calculate volumes and mass by numerical integration. End diastole was defined as the first image in the ECG triggered sequence and end systole (ES) was the image with the smallest left ventricular cavity area. The difference between epicardial and endocardial volumes was multiplied by the specific gravity of myocardium (1.05 g/ml) and averaged over the cardiac cycle in order to obtain left ventricular mass. The above method does not use geometrical assumptions and enables left ventricular mass to be calculated more accurately than by other methods such as echocardiography (Rajappan et al., 2000).

Apical Rotation

The apex was defined as the third of the ventricle furthest from the mitral annulus. The most apical slice had its apical edge positioned on the endocardium at the apex, and this slice was used in measurements of apical rotation. Positive apical rotation was defined as the number of degrees of anticlockwise rotation of the apex about the centroid of the left ventricular cavity (Nagel et al., 2000; Stuber et al., 1999).

Strain Analysis

In the analysis of left ventricular strain, or percent shortening, end diastole was taken to be the first image after the R wave and end systole was taken to be the frame of least model volume in the tagged image series. Prolonged relaxation was identified by comparing the amount of strain persisting at a particular time after end systole (e.g., 150% of ES) or the time taken to relax to 50% of peak value in one group relative to the other. The maximum speed of relaxation was determined by the peak strain-rate after end systole.

Torsion

Torsion is a measure of the degree of twist in the myocardium about the left ventricular long axis. During myocardial contraction, the base of the heart rotates in an opposite direction to the apex. We defined cardiac torsion as the change in angle between two line segments initially oriented in the longitudinal (L) and circumferential (C) directions. Both the distance between the apex and base as well as relative rotation of the apex affect this measurement, and both may vary among individuals and during the cardiac cycle (Stuber et al., 1999). Torsion angle (α) was calculated from the Lagrangian strain tensor E in the following standard mathematical equation for calculating strain (Fung, 1977).

$$\sin \alpha_{CL} = \frac{2E_{CL}}{\sqrt{1+2E_{CC}}\sqrt{1+2E_{LL}}} \tag{1}$$

Circumferential Strain

Average left ventricular circumferential strain, or shortening, describes the size of the left ventricular circumference relative to its initial length. Percentage circumferential shortening ($\%\, S_C$) was calculated from the Lagrangian strain tensor E (Fung, 1977) as

$$\%\, S_C = (\sqrt{(1+2E_{CC})} - 1) \times 100\% \tag{2}$$

This was determined at multiple points in the cardiac cycle by fitting a three-dimensional finite element model to the data and was expressed as a percentage of maximum shortening. Shortening was generally maximal at end systole, and this corresponds to 100% on the time axis (Fig. 3).

Longitudinal Strain

Longitudinal motion was measured parallel to the long axis of the left ventricle. Average longitudinal strain or shortening, ($\%S_L$) describes the length of the left ventricle as a percentage of its initial length and was calculated from the Lagrangian strain tensor E (Fung, 1977) as

$$\%S_L = (\sqrt{(1 + 2E_{LL})} - 1) \times 100\% \quad (3)$$

Statistical Analysis

Data were analyzed using Students' t-test to compare the degree of apical rotation, torsion, and circumferential and longitudinal shortening through most of the cardiac cycle among the two groups. All tests were two-tailed and a 5% significance level was maintained throughout. To assess the effect of systolic blood pressure or mass-to-volume ratio in the older compared with the young group, analyses of covariance of the peak rates of relaxation were performed.

RESULTS

Thirty-three subjects were screened (15 young, 18 old). Two subjects from the older group were excluded, one after an inferior wall motion abnormality was identified on transthoracic echocardiography and another because of coexisting cryptogenic fibrosing alveolitis. Approximately three-quarters of each group were male. The mean age of the young group was 46 years younger than the older group. Systolic and diastolic blood pressures were significantly higher in the older compared with the young group (Table 1). For all subjects included in the study, tagged stripes could be analyzed throughout the imaged cycle.

Left Ventricular Mass and Volumes

There were no significant differences in either left ventricular mass or ejection fraction between the two groups (Table 2). Left ventricular end-diastolic volume was significantly smaller in the older compared with the young group, and the ratio of left ventricular mass to end diastolic volume was significantly greater in the older compared with the young group.

Apical Rotation and Torsion

Peak apical rotation was significantly greater in the old group ($p = 0.003$), as was peak torsion angle ($p < 0.001$) (Table 3). Figure 2 shows apical rotation as a function of time indexed to end systole. At 150% of end systole, apical rotation was significantly higher in the older group (Table 3). During myocardial relaxation, the time taken for apical rotation to reduce to 50% of its peak value was significantly longer in the older compared with the young group, ($p = 0.007$). The peak velocity of apical rotation during diastole was similar between the two groups (Table 3); however, the normalized relaxation velocity, i.e., the ratio of peak velocity to peak rotation value was reduced in the older group (-5.1 ± 1.2 vs. $-6.7 \pm 1.2°/s$, $p = 0.001$).

Circumferential Strain

Peak strain in the circumferential direction, (% Sc) was not significantly different between the two groups ($p = 0.085$). However, it took significantly longer for

Table 2. Mass and volume measurements.

	Young (n = 15) Mean (SD)	Old (n = 16) Mean (SD)	p value
Mass, g	143.0 (34.1)	146.0 (38.7)	0.82
Ejection fraction, %	70.7 (3.0)	69.3 (6.6)	0.46
Stroke volume, ml	97.1 (18.8)	79.8 (19.5)	0.018*
End systolic volume, ml	40.4 (9.2)	35.8 (12.7)	0.259
End diastolic volume, ml	137 (26.7)	115 (27.1)	0.031*
Mass: EDV ratio	1.04 (0.10)	1.28 (0.30)	0.006*

EDV: end diastolic volume.
*$p < 0.05$.

Table 3. Material motion and relaxation parameters mean (SD).

		PV	150% ES	PRR	T 50% (ms)
Old	Apex rot.	13.9 (2.2)°[a]	5.8 (2.2)°[b]	71.0 (21.1)°/s	149 (50)[a]
	Torsion	6.5 (1.0)°[c]	2.8 (0.9)°[b]	36.4 (8.1)°/s	174 (99)
	% S_C	18.7 (3.1)%	12.0 (2.9)%[b]	76.2 (28.5)%/s[c]	234 (49)[c]
	% S_L	15.5 (2.5)%	10.5 (2.0)%[b]	62.7 (21.3)%/s[c]	228 (61)[a]
Young	Apex rot.	10.9 (3)°	3.0 (1.9)°	71.0 (19.2)°/s	109 (19)
	Torsion	5.1 (1.1)°	1.8 (0.9)°	31.8 (10.1)°/s	130 (41)
	% S_C	20.2 (1.1)%	8.2 (3.1)%	142.5 (16.6)%/s	155 (16)
	% S_L	16.9 (1.3)%	7.9 (3.2)%	122.5 (19.6)%/s	174 (24)

Apex Rot.: Apex rotation, % S_C: % circumferential shortening, % S_L: % longitudinal shortening, 150% ES: value at 150% of end systole, PRR: peak rate of relaxation, PV: peak value, T 50%: time from peak to 50% of peak.
[a] $p < 0.01$.
[b] $p < 0.05$.
[c] $p < 0.001$.

circumferential strain to reduce to 50% of its peak value in the older compared with the young group ($p = 0.001$) (Fig. 3). The peak rate of change of circumferential strain, i.e., lengthening velocity, was significantly slower in the older group ($p < 0.001$) so that at 150% of end systole significantly more %Sc persisted in the older compared with the young group ($p < 0.05$) (Table 3).

Longitudinal Strain

Peak longitudinal strain (% S_L) tended to be reduced, but did not significantly differ in the older compared with the young group ($p = 0.053$) (Table 3). The peak lengthening strain rate was reduced ($p < 0.001$) and time to 50% of peak value was increased ($p < 0.01$) in the older group. Accordingly, significantly more longitudinal strain persisted at 150% of end systole in the older compared with the young group (Fig. 4).

DISCUSSION

During myocardial relaxation and diastole, the left ventricular myocardium performs a complex movement involving rotational, circumferential, and longitudinal

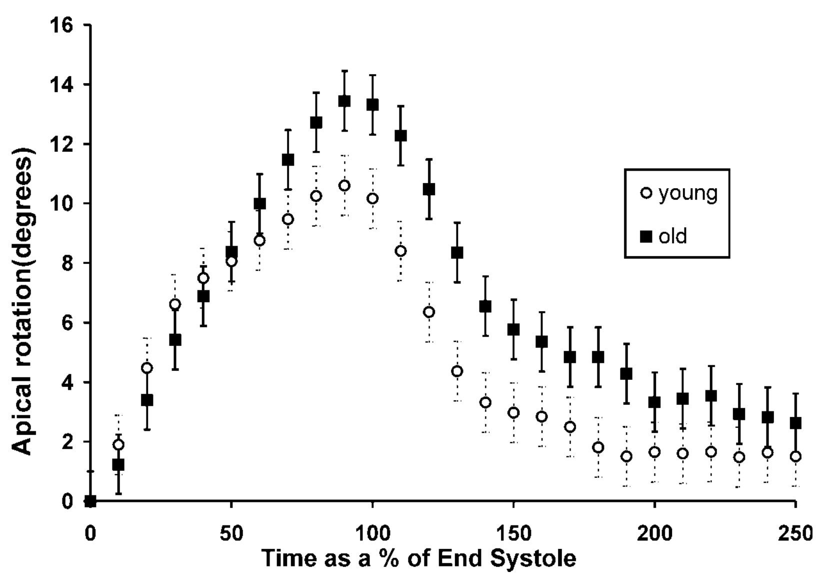

Figure 2. Apical rotation in young and older normal volunteers.

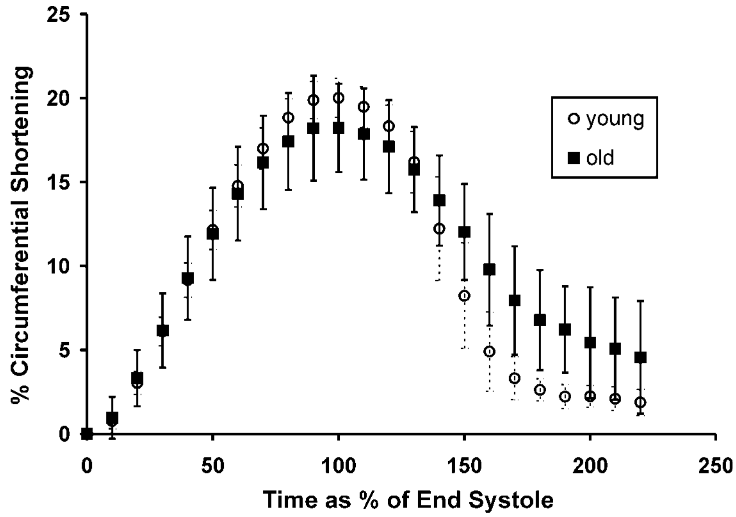

Figure 3. Circumferential shortening as a function of time to end systole. Values for shortening were expressed relative to the time to end systole in order to overcome differences in heart rates between the subjects.

motion. Full assessment therefore requires visualization and analysis of all these movement components. Although measurement of diastolic performance is increasingly recognized as an important part in the assessment of cardiac function, standard imaging techniques are hindered by an inability to image the heart in three dimensions or to directly assess myocardial motion. Measures of diastolic function often rely on assessing blood flow into the ventricles rather than measuring the properties of the myocardium itself. Magnetic resonance imaging, however, is able to examine the motion of the myocardium directly and in three dimensions throughout systole and most of diastole.

Mass and Volume

An increase in left ventricular mass is often reported to be associated with advancing age but was not seen in this study. Autopsy studies have suggested that

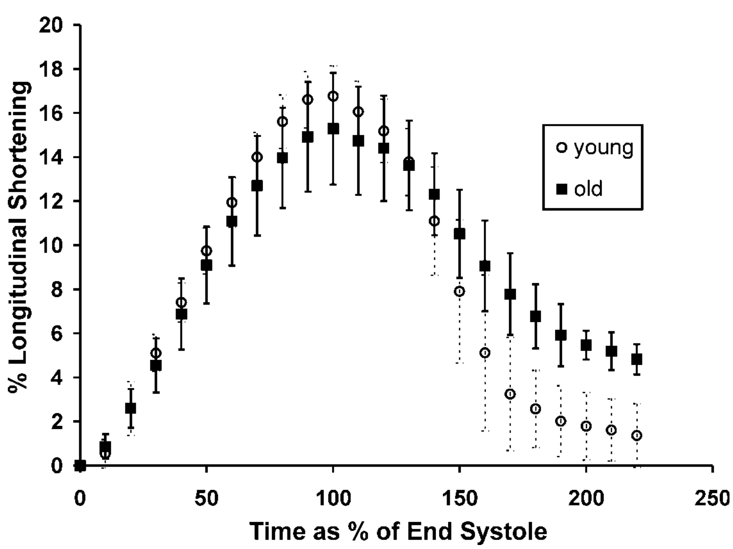

Figure 4. Longitudinal shortening as a function of time to end systole.

coexisting disease rather than advancing age per se causes increased mass in older people and is not seen in normal older individuals (Kitzman et al., 1988). Although the numbers included in this study are small, MRI is an accurate method to measure left ventricular mass and volume (Lorenz et al., 1999). The increase in mass-to-volume ratio in the older group has been noted previously (Lakatta, 2000), is correlated with blood pressure ($R^2 = 0.37$, $p < 0.001$), and may be due to increased afterload.

Systole

In individuals carefully screened to exclude coexisting disease, resting left ventricular systolic function is thought to be unaffected by aging (Kitzman et al., 1991; Lakatta, 1993; Nichols et al., 1985; Yamakado et al., 1997). No significant differences in global systolic chamber function, assessed by left ventricular ejection fraction, were observed between the two groups in this study. Although peak apical rotation and torsion were increased in the older group, peak longitudinal and circumferential strains were not significantly different. Similar findings using MRI with tagging have been described in people with left ventricular hypertrophy secondary to aortic stenosis (Nagel et al., 2000; Stuber et al., 1999) and in patients with hypertrophic cardiomyopathy (Young et al., 1994). No correlation between apical rotation or torsion and mass-to-volume ratio was found, but both peak $\%S_C$ and peak $\%S_L$ decreased with increased mass-to-volume ratio ($R^2 = 0.39$, $p < 0.001$ and $R^2 = 0.53$, $p < 0.001$, respectively). Whilst changes in mass-to-volume ratio may account for differences seen at end systole, they do not explain the differences observed during myocardial relaxation and diastole.

Myocardial Relaxation and Diastole

More circumferential and longitudinal strain persisted into diastole, together with increased apical rotation and ventricular torsion in the older group. Thus, in this group, the ventricle is partially rotated and contracted, whilst younger individuals have an almost fully untwisted and relaxed ventricle during the same time period. In a study of patients with aortic stenosis, MRI tagging identified delayed reversal of apical rotation and a decreased, normalized rotation velocity during diastole (Nagel et al., 2000; Stuber et al., 1999). Our results indicate that increasing torsion, together with reduced relaxation strain rates also occur to some degree due to aging in healthy volunteers, highlighting the need for age-matched controls in studies of diastolic function. In this study, peak $\%S_C$ and $\%S_L$ lengthening velocities decreased with increasing mass-to-volume ratio ($R^2 = 0.56$, $p < 0.001$ and $R^2 = 0.43$, $p < 0.001$, respectively); however, analysis of covariance showed that these strain rates were still significantly lower in the older group after correcting for differences in mass-to-volume ratio ($p < 0.001$ in each case). It is possible that the differences in strain rates were due to the different blood pressures seen between the groups. However, mass-to-volume ratio, which correlated significantly with blood pressure, was not accountable for all of the differences in diastolic strain between the groups. In an analysis of covariance on the peak rates of relaxation and systolic blood pressure, the effect of the group was still present after correcting for either systolic or diastolic blood pressure. However, taken across both groups there was a correlation with systolic blood pressure. Thus, larger numbers of subjects with a greater range of blood pressures would be needed to prove that blood pressure was the cause of the changes seen in diastole with advancing age.

Doppler echocardiography identified significant differences in both early (E) and late (A) transmitral flow velocities between the two groups (Table 1). Previous reports have also identified reduced blood flow during early diastole in older compared with young individuals (Benjamin et al., 1992; Kitzman et al., 1991; Pearson et al., 1991; Spirito and Maron, 1988). This reduction in early diastolic filling is thought to be due, in part, to an intrinsic aging process that affects left ventricular compliance (Kitzman et al., 1991). Blood will flow less freely into a partially contracted and rotated ventricle than into one that is fully relaxed. By including longitudinal and circumferential movement together with apical rotation and torsion into the study, observations using MRI have been extended to a full, three-dimensional description of myocardial motion. Thus, MRI with tagging is able to observe changes in three-dimensional myocardial motion that describe a mechanism that could explain the delayed, reduced early left ventricular filling previously identified using echocardiography. Changes in myocardial relaxation and diastole are sensitive markers of myocardial disease or dysfunction (Yun et al., 1991), and previous studies have suggested that torsion may be less volume and load-dependent than current techniques as a measure of diastolic function (Dong et al., 1999; Hansen et al., 1991).

Previous studies have described a prolongation of apical untwisting during relaxation and diastole in patients with severe left ventricular hypertrophy (Nagel et al., 2000) or hibernating myocardium (Matter et al., 1996), but a prolongation of material relaxation associated with increasing age has not previously been described. Prolonged myocardial relaxation has been described in senescent rats and is thought to be due to reduced uptake of calcium into the sarcoplasmic reticulum (Tate et al., 1990). This study supports observations made in animals, that the aging process is associated with a prolongation of myocardial relaxation.

Limitations of the Study

Conclusive evidence of the absence of important coronary occlusive disease was not obtained by performing coronary angiography on the older study participants. Thus, coexisting occult cardiac disease may have accounted for some of the differences seen between the groups. Changes in myocardial relaxation cannot be assumed to be associated with reduced early diastolic flow, because simultaneous measurement of left ventricular filling and myocardial movement was not performed. However, echocardiographic assessment did confirm a reduction in the peak early diastolic filling velocity in the older compared with the young group (Table 1). Also, newer echocardiographic measurements of diastolic function, such as tissue Doppler imaging, were not available for inclusion in this analysis. Alterations in the tagging sequence may improve tag stripe resolution and persistence in future studies and allow better acquisition of the atrial component of left ventricular filling. Although the labor intensive off-line analysis continues to be a limiting factor for routine clinical evaluation of tagged MRI images, this technique may play an important role in the assessment of myocardial relaxation and diastolic function in the future.

CONCLUSIONS

Magnetic resonance imaging with tagging can be used to quantify three-dimensional myocardial motion through most of the cardiac cycle. Myocardial relaxation is significantly delayed and reduced in older normal individuals as evidenced by a persistence of apical rotation, circumferential and longitudinal strain, and slower rates of lengthening and reversal of apical rotation.

REFERENCES

Axel, L., Dougherty, D. (1989). Heart wall motion: improved method of spatial modulation of magnetisation for MR imaging. *Radiology* 172:349–350.

Benjamin, E. J., Levy, D., Anderson, K. M., Wolf, P. A., Plehn, J. F., Evans, J. C., Comai, K., Fuller, D. L., Sutton, M. S. (1992). Determinants of Doppler indexes of left ventricular diastolic function in normal subjects (the Framingham Heart Study). *Am. J. Cardiol.* 70:508–515.

Dong, S. J., Hees, P. S., Huang, W. M., Buffer, S. A. Jr., Weiss, J. L., Shapiro, E. P. (1999). Independent effects of preload, afterload, and contractility on left ventricular torsion. *Am. J. Physiol.* 277:H1053–H1060.

Fung, Y. C. (1977). *A First Course in Continuum Mechanics*. 2nd ed. Englewood Cliffs, NJ: Prentice Hall, Inc., pp. 127–135.

Hansen, D. E., Daughters, G. T., Alderman, E., Ingels, N. B., Stinson, E., Miller, D. C. (1991). Effect of volume loading, pressure loading and inotropic stimulation on left ventricular torsion in humans. *Circulation* 83:1315–1326.

Kitzman, D., Scholz, D., Hagen, P., Ilstrup, D., Edwards, W. (1988). Age-related changes in normal human hearts during the first ten decades of life. Part II (maturity): a quantitative anatomic study of 765 specimens from subjects 20 to 99 years old. *Mayo Clin. Proc.* 63:137–146.

Kitzman, D., Sheikh, K., Beere, P., Philips, J., Higginbotham, M. (1991). Age-related changes of Doppler left ventricular filling indexes in normal subjects are independent of left ventricular mass, heart rate, contractility and loading conditions. *J. Am. Coll. Cardiol.* 18:1243–1250.

Lakatta, E. (1993). Cardiovascular regulatory mechanisms in advanced age. *Physiol. Rev.* 73:413–467.

Lakatta, E. G. (2000). Cardiovascular aging in health. *Clin. Geriatr. Med.* 16:419–444.

Lorenz, C., Walker, E., Morgan, V., Klein, S., Graham, T. (1999). Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. *J. Cardiovasc. Magn. Reson.* 1:7–21.

Matter, C., Nagel, E., Stuber, M., Boesiger, D., Hess, O. (1996). Assessment of systolic and diastolic LV function by MR myocardial tagging. *Basic Res. Cardiol.* 91(Suppl. 2):23–28.

Moon, M., Ingels, N. B., Daughters, G. T., II, Stinson, E., Hansen, D., Miller, C. (1994). Alterations in left ventricular twist mechanics with inotropic stimulation and volume loading in human subjects. *Circulation* 89:142–150.

Nagel, E., Stuber, M., Burkhard, B., Fisher, S. E., Scheidegger, M. B., Boesiger, P., Hess, O. M. (2000). Cardiac rotation and relaxation in patients with aortic stenosis. *Eur. Heart J.* 21:582–589.

Nichols, W., O'Rourke, M., Avolio, A., Yaginuma, T., Murgo, J., Pepine, C., Conti, C. R. (1985). Effects of age on ventricular-vascular coupling. *Am. J. Cardiol.* 55:1179–1184.

Pearson, A., Gudipati, C., Nagelhout, D., Sear, J., Cohen, J., Labovitz, A. (1991). Echocardiographic evaluation of cardiac structure and function in elderly subjects with isolated systolic hypertension. *J. Am. Coll. Cardiol.* 17:422–430.

Rademakers, F. E., Bogaert, J. (1997). Left ventricular myocardial tagging. *Int. J. Cardiac Imaging* 13:233–245.

Rademakers, F., Buchalter, M., Rogers, W. (1992). Dissociation between left ventricular untwisting and filling. Accentuation by catecholamines. *Circulation* 85:1572–1581.

Rajappan, K., Bellenger, N. G., Anderson, L., Pennell, D. J. (2000). The role of cardiovascular magnetic resonance in heart failure. *Eur. J. Heart Failure* 2:241–252.

Spirito, P., Maron, B. J. (1988). Influence of aging on Doppler echocardiographic indices of left ventricular diastolic function. *Br. Heart J.* 59:672–679.

Stuber, M., Scheidegger, M., Fischer, S., Nagel, E., Steinemann, F., Hess, O. M., Boesiger, P. (1999). Alterations in the local myocardial motion pattern in patients suffering from pressure overload due to aortic stenosis. *Circulation* 100:361–368.

Tate, C. A., Taffet, G. E., Hudson, E. K., Blaylock, S. L., McBride, R. P., Michael, L. H. (1990). Enhanced calcium uptake of cardiac sarcoplasmic reticulum in exercise-trained old rats. *Am. J. Physiol.* 258:H431–H435.

Wei, J. (1992). Age and the cardiovascular system. *N. Engl. J. Med.* 327:1735–1739.

Yamakado, T., Takagi, E., Okubo, S., Imanaka-Yoshida, K., Tarumi, T., Nakamura, M., Nakano, T. (1997). Effects of aging on left ventricular relaxation in humans. Analysis of left ventricular isovolumic pressure decay. *Circulation* 95:917–923.

Young, A., Kramer, C., Ferrari, V., Axel, L., Reichek, N. (1994). Three-dimensional left ventricular deformation in hypertrophic cardiomyopathy. *Circulation* 90: 854–867.

Young, A., Kraitchman, D., Dougherty, L., Axel, L. (1995). Tracking and finite element analysis of stripe deformation in magnetic resonance tagging. *IEEE Trans. Med. Imaging* 14:413–421.

Yun, K. L., Niczyporuk, M. A., Daughters, G. T., Ingels, N. B., Stinson, E. B., Alderman, E. L., Hansen, D. E., Miller, D. C. (1991). Alterations in left ventricular diastolic twist mechanics during acute human cardiac allograft rejection. *Circulation* 83:962–973.

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